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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,145	06/19/2003	Sang-Yup Lee	HYLEE80.001C1	5042

20995 7590 03/13/2006

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EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/600,145	LEE ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 4 pgs

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/20/03*.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-24 are pending in the present application.

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in 2001-0048881 Republic of Korea on August 14, 2001. It is noted, however, that applicant has not filed a certified copy of the 2001-0048881 Republic of Korea application as required by 35 U.S.C. 119(b).

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in PCT/KR02/01547 on August 13, 2002. It is noted, however, that applicant has not filed a certified copy of the PCT/KR02/01547 application as required by 35 U.S.C. 119(b).

3. Claims 1-14 are objected to because of the following informalities: claim 1, line 1, there is a hypen/dash ("comprising,-an OmpF"); is this what Applicants intend? Appropriate correction is required.

4. Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-14 are vague and indefinite in the recitation of "fragment" (see line 3). Does this fragment refer to the fragment of the OmpF gene as set forth in line 1 of claim 1 or is this a fragment of the gene of interest? Claims 15-24 are vague and indefinite in the recitation of "introducing the protein of interest into the vector of claim 1". Does mean that the gene that encodes that protein of interest? The same is applied to claim 6, do Applicants intend that the gene of interest can encode the protein of interest?

With regard to claim 1, lines 3-4, "said expression vector produces an OmpF fusion protein fused with the gene of interest". This is unclear; is the fusion protein a fusion of the OmpF protein and any protein, peptide, enzyme or antibody or is it OmpF protein fused to the gene of interest?

5. The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure for the claimed invention. It is apparent that the expression vector pOmpF6 (accession number KCTC 1026BP) is required to practice the claimed invention. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the above plasmids. See 37 C.F.R. 1.802.

The specification does not provide a repeatable method for obtaining the attenuated strain and it does not appear to be readily available material. Deposit of the strains would satisfy the enablement requirements of 35 U.S.C. § 112. If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R. 1.808.

If the deposits have not been made under the provisions of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of the application, access to the deposits will be afforded to one determined by the Commissioner to be entitled thereto;
(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;
© the deposits will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;
(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and
(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

6. Claims 1-24 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification. It appears that Applicants may have already deposited the plasmids, however the information is not complete. The deposit information as required by the Budapest Treaty has not been made. In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-7, 9-11, 15, 17, 18 and 20-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Mizushima et al (EP 0138644 B1).

Mizushima et al discloses vectors and a host to harbor the vector and that the vector is suitable for use in the expression of proteins and secretion of the expressed protein out of the host microbial cell (p. 2; claims). The prior art discloses that the OmpF protein is an outer membrane protein of *E. coli* and is one of the proteins produced most abundantly in *E. coli*. Mizushima et al discloses an expression vector containing the OmpF protein attached to a foreign polypeptide, which could be an enzyme (p. 2). The prior art "provides a plasmid vector comprising a fragment which comprises the regulator region containing the ompF

promoter of a Gram-negative bacterium, the region coding for the signal peptide of the OmpF protein and up to 30 nucleotides of the ompF structural gene, the fragment being inserted into a relaxed plasmid derived from *E. coli*. The invention also provides *E. coli* strain suitable for use as a host of the vector." (p. 2, l. 28-32) "The plasmid vector of the invention, which is obtained by insertion of the specified fragment containing the ompF promoter into a relaxed plasmid found in multiple copies per cell in E. coli, may be suitable for use as an expression vector. The expression vector may be constructed by inserting a heterologous gene 50 coding for a useful protein having a physiological activity into an appropriate restriction site which is found downstream near the promoter. Such a cleavage site may be the restriction site at the 3'-terminus of the specified fragment containing the ompF promoter (BglII site or the like), the restriction site in the synthetic linker (EcoR1 site or the like) when used, or an appropriate site in the relaxed plasmid which is downstream near the specified fragment. In order to ensure the expression of the heterologous gene, transcription and translation of the heterologous gene should be under the control of the ompF promoter..." (p. 3, l. 47-56) The vector is introduced in a host of E. coli to produce the protein. "Such E. coli host may be cultured and transformed with the plasmid vector by any conventional method. The use of the plasmid vector containing the ompF gene, in which the fragment containing the ompF promoter comprises the gene coding for the signal peptide of the OmpF protein and a part of the structural gene of the OmpF protein downstream of the ompF promoter, provides the desired protein in the form of a stable fused protein comprising a part of the OmpF protein at the N-terminus. The ompF promoter is such a strong promoter that the gene coding for the protein to be obtained is efficiently transcribed and translated. On the other

hand, the signal peptide of the OmpF protein enhances the secretion of the expressed protein out of the cytoplasmic membrane and, therefore, facilitates the separation and purification of the protein produced." (p. 4, l. 16-25) Example 3 of the prior art discloses that the expressed foreign protein is β-endorphin (p. 5). The selectable marker was ampicillin resistance and the protein was purified from the culture medium by concentration, desalting and HPLC (p. 8).

The prior art discloses the claimed expression vector and method of producing a protein of interest. Since the Patent Office does not have the facilities for examining and comparing applicants' expression vector and methods of producing proteins of interests with the expression vector and methods of producing proteins of interests of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed expression vector and methods of producing proteins of interests and the expression vector and methods of producing proteins of interests of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

12. Claims 1-3, 6, 7, 9-11, 15, 17, 18, 22 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Nagahari et al (EMBO Journal, 1985, 4/13A:3589-3592).

Nagahari et al discloses a plasmid constructed in which the structural gene for human β-endorphin is preceded by the upstream region of the ompF gene consisting of the promoter region and the coding regions for the signal peptide and the N terminus of the OmpF protein (abstract). When the plasmid was introduced into E. coli, an OmpF-β-endorphin fused peptide was synthesized and secreted into

the culture medium through both the cytoplasmic and outer membranes (abstract; p. 3589, right column; p. 3591, right column). Nagahari et al discloses an expression vector that contains the selectable marker, ampicillin resistance (Figure 1, p. 3590). The produced proteins were purified by reverse-phase HPLC (figure 3, p. 3591; materials and methods p. 3592, left column).

The prior art discloses the claimed expression vector and method of producing a protein of interest. Since the Patent Office does not have the facilities for examining and comparing applicants' expression vector and methods of producing proteins of interests with the expression vector and methods of producing proteins of interests of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed expression vector and methods of producing proteins of interests and the expression vector and methods of producing proteins of interests of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

13. Claims 1-7, 9-13, 15-18 and 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizushima et al (EP 0138644 B1) taken with Simula et al (Toxicology, 1993, 82/1-3:3-20, abstract only)

Mizushima et al discloses vectors and a host to harbor the vector and that the vector is suitable for use in the expression of proteins and secretion of the expressed protein out of the host microbial cell (p. 2; claims). The prior art discloses that the OmpF protein is an outer membrane protein of *E. coli* and is one of the proteins produced most abundantly in *E. coli*. Mizushima et al discloses an expression vector containing the OmpF protein attached to a foreign polypeptide,

which could be an enzyme (p. 2). The prior art "provides a plasmid vector comprising a fragment which comprises the regulator region containing the ompF promoter of a Gram-negative bacterium, the region coding for the signal peptide of the OmpF protein and up to 30 nucleotides of the ompF structural gene, the fragment being inserted into a relaxed plasmid derived from *E. coli*. The invention also provides *E. coli* strain suitable for use as a host of the vector." (p. 2, l. 28-32) "The plasmid vector of the invention, which is obtained by insertion of the specified fragment containing the ompF promoter into a relaxed plasmid found in multiple copies per cell in E. coli, may be suitable for use as an expression vector. The expression vector may be constructed by inserting a heterologous gene 50 coding for a useful protein having a physiological activity into an appropriate restriction site which is found downstream near the promoter. Such a cleavage site may be the restriction site at the 3'-terminus of the specified fragment containing the ompF promoter (BglII site or the like), the restriction site in the synthetic linker (EcoR1 site or the like) when used, or an appropriate site in the relaxed plasmid which is downstream near the specified fragment. In order to ensure the expression of the heterologous gene, transcription and translation of the heterologous gene should be under the control of the ompF promoter..." (p. 3, l. 47-56) The vector is introduced in a host of E. coli to produce the protein. "Such E. coli host may be cultured and transformed with the plasmid vector by any conventional method. The use of the plasmid vector containing the ompF gene, in which the fragment containing the ompF promoter comprises the gene coding for the signal peptide of the OmpF protein and a part of the structural gene of the OmpF protein downstream of the ompF promoter, provides the desired protein in the form of a stable fused protein comprising a part of the OmpF protein at the N-

terminus. The ompF promoter is such a strong promoter that the gene coding for the protein to be obtained is efficiently transcribed and translated. On the other hand, the signal peptide of the OmpF protein enhances the secretion of the expressed protein out of the cytoplasmic membrane and, therefore, facilitates the separation and purification of the protein produced." (p. 4, l. 16-25) Example 3 of the prior art discloses that the expressed foreign protein is β-endorphin (p. 5). The selectable marker was ampicillin resistance and the protein was purified from the culture medium by concentration, desalting and HPLC (p. 8).

Mizushima et al discloses the claimed invention except for the teaching that *Salmonella* sp. can be the host microorganism. However, Simula et al teaches that heterologous expression of recombinant proteins via expression vectors in either *E. coli* of *S. typhimurium* (abstract). It is well known in the state of the art that salmonella can be used as a host microorganism; the expression vector containing the genes of interest for example. It would have been obvious to a person of ordinary in the skill of the art at the time the invention was made to use both Mizushima et al and Simula et al for what they teach as a whole with the reasonable expectation of success of producing proteins of interest or in making an expression vector. The claimed invention is prima facie obvious in view of the combined teachings of the prior art absent any convincing evidence to the contrary.

14. No claims are allowed.

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
March 6, 2006